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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,036	12/10/2001	Michel Koehl	017753-150	8634

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EXAMINER

CHEN, STACY BROWN

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,036	KOEHL ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>10-22-2003</u> | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's amendment filed October 22, 2003 is acknowledged and entered. Claims 19-38 are pending and examined.
2. All prior rejections under 35 U.S.C. 112, second paragraph, 102(b) and 103(a) are moot in view of Applicant's cancellation of claims 1-18.

Claim Objections

3. Claims 19 and 32 are objected to because of the following informalities:
 - In claim 19, section a, there should be an "a" before "fluidized bed".
 - In claim 32, the preamble recites "A protocol or producing", but should recite "A protocol for producing".

Claim Rejections - 35 USC § 112

4. Claims 20, 21, 35 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The use of the trademarks Streamline®XL, Streamline®Q XL, Toyopearl®HW65F, Toyopearl®S, Sephacryl™S400HR and Tween®80, respectively, render the claims indefinite because the formulas of the products may change at any time, thereby altering the composition being claimed. The claims must recite the generic terminology in place of the trademark in order to overcome the rejection. Further, claims 20 and 21 recite "Streamline®XL type" and "Streamline®Q XL type", which is indefinite because the

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characteristics that are retained in a “type” are not disclosed. Suggested language is the generic terminology and the omission of “type”.

Claim Rejections - 35 USC § 103

5. Claims 19-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shabram *et al* (WO 96/27677 A2), of record, in view of Berg *et al* (WO 98/33572 A1). The claims are drawn to a method for purifying adenoviral particles from a crude viral preparation comprising contacting the preparation with particles of adsorbent in a fluidized bed, eluting the adsorbed adenoviral particles from the adsorbent particles and collecting the eluted adenoviral particles. The particles of adsorbent are comprised of an agarose matrix and a central core comprising quartz (Streamline®XL type or Streamline®Q XL type). Dextran chains are covalently coupled to the matrix, and positively charged groups (Q groups) are attached to the matrix. The yield of adenoviral particles is approximately 80% or higher. The adsorbent particles can be of heterologous sizes. During the contacting step of the method, the pH is approximately 8.5, and the step is carried out in a buffer equilibrated at a final NaCl concentration of 400mM. The conductivity conditions are between approximately 30-35 mS/cm. The eluting step is carried out by increasing the salinity. Also claimed is a protocol for producing adenoviral particles comprising producing a crude viral preparation by infecting or transfecting a cell line with an adenoviral vector (recombinant and replication defective), culturing the cell line and purifying the adenoviral particles according to the method outlined above. The cell can be ruptured or lysed after collecting the cells from culture, optionally followed by degradation of nucleic acids and inactivation. Packed bed gel filtration chromatography can be carried out on a support

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comprising beads with a diameter of between 10 and 80 micrometers. The support can be Toyopearl®HW65F, Toyopearl®S, or Sephacryl™S400HR. The inactivation step can be accomplished with a mixture of TNBP and Tween®80.

6. The teachings of Shabram are of record. To summarize, Shabram teaches a method of purifying recombinant adenoviruses (viral vectors for use in gene therapy) from a cell lysate comprising two chromatography steps (fluidized-bed adsorption), see abstract, page 8, lines 4-8, and page 9, lines 13-15. Shabram uses a cross-linked agarose column (page 11, lines 27-28). The salt concentration of the eluant is diluted to about 450 millimolar or less in order to prevent premature stripping of viral particles from the exchange resin (page 12). A buffer is used to maintain the pH of the cell lysate solution between about 5.0 and 9.0. During chromatography, the resins are treated by flushing with NaCl and water. Shabram also discloses the production of adenoviral vectors from cell lines (page 15), lysis (page 17) and nucleic acid degradation (page 18). Shabram fails to teach the specific type of adsorbent particle as instantly claimed, and the overall yield of approximately 80% or higher.

7. However, Berg teaches a method for adsorption of a substance from a liquid sample on a fluidized bed, in which the total yields are improved. The beads used in the method comprise a structure/ligand linked to a base matrix (bead) via an extender. The base matrix is comprised of cross-linked agarose (page 8, lines 28-33) and a bead filler of quartz (page 9, lines 30-31). Dextran is covalently bound to the agarose matrix (page 5, lines 2-17).

8. It would have been obvious to modify Shabram's method with the adsorbent particles of Berg. One would have been motivated to use Berg's adsorbent particles because Berg's method is aimed at improving total yields and productivity in adsorption processes on fluidized beds, and

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providing filler matrices that have improved breakthrough capacity in fluidized beds (page 4, lines 15-21). One would have had a reasonable expectation of success that the adsorbent particles of Berg would have improved Shabram's method because Berg's particles are intended for use in methods of adsorption using fluidized beds. Further, one would have expected that using Berg's particles would have resulted in an improved yield over Shabram's 67%.

Applicant's argues in the response filed October 22, 2003, that Shabram's yield of total adenoviral particles is less than Applicant's yield of approximately 80% or higher. While the Office recognizes that the yield of Shabram is lower than Applicant's yield, one of ordinary skill in the art would have expected a higher yield using the method of Berg. Applicant's claim to "approximately 80%" yield could encompass Shabram's 67%, and certainly any increase in yield over Shabram's 67%, as expected with the use of Berg's particles, would fall within the scope of "approximately 80%".

9. In Applicant's response of October 22, 2003, Applicant argues that Shabram mentions only the possibility of performing the chromatographic steps in fluidized bed columns, while only illustrating conventional packed bed columns. In response, the Office considers Shabram's mention of the possibility of performing the chromatographic steps in fluidized bed columns to be sufficient for disclosing the claimed invention. While Shabram may have only illustrated conventional packed bed columns, one of ordinary skill would have been motivated to use fluidized bed columns by Shabram's teaching on page 9, lines 13-15.

Conclusion

10. No claim is allowed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 872-9306. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy B. Chen, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday from 7:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SBC

Stacy B. Chen
December 18, 2003

James C. Housel
JAMES HOUSEL 12/26/03
SUPERVISORY PATENT EXAMINER
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